REMARKS

This amendment responds to the office action mailed December 26, 2002. Claims 1-9, 17, 20, 23-31 and 73-79 were pending in the instant Application. With the instant amendment, Claims 1-9, 17, 20 and 74-79 have been canceled without prejudice, as drawn to non-elected subject matter. Claims 23-31 and 73 have been canceled, without prejudice, and replaced by new Claims 80-98. Thus, after entry of the instant amendment, Claims 80-98 are pending and under consideration.

New Claims 80-98 are fully supported by the specification and the claims as originally filed. Support for new Claims 80-83 can be found in the specification at, for example, page 9, lines 6-12, and in Claim 23 as originally filed. Support for new Claims 84-87 can be found in, for example, Claims 24-27, respectively, as originally filed. Support for new Claims 88-91 can be found in the specification at, for example, page 88, line 34, through page 89, line 2, and in Claim 28 as originally filed. Support for new Claims 92 and 93 can be found in, for example, Claims 29 and 30, respectively, as originally filed. Support for new Claims 94-97 can be found in, for example, Claim 31 as originally filed. Support for new Claim 98 can be found in the specification at, for example, page 46, lines 3-14, and page 87, line 1, through page 89, line 14, especially at page 87, lines 10-13.

Applicant expressly reserves the right to pursue any canceled subject matter in one or more related, continuation, divisional or continuation-in-part application(s).

Applicant acknowledges the Draftsperson's objection to the drawings under 37 CFR §§ 1.84 or 1.52 and the reminder that formal drawings will be required when the application is allowed.

I. THE REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 23-31 and 73-79 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. As pointed out, above, none of Claims 23-31 and 73-79 are currently pending. However, for the reasons set forth below, Applicant asserts that the pending claims are definite under 35 U.S.C. §112, second paragraph.

The PTO bases its rejection of Claims 23-31 and 73-79 on the contention that "reference to 'HIV-infected' patient and 'HIV reverse transcriptase' is vague and ambiguous

. . . [because] it is not readily manifest if applicant is detecting mutational changes in the HIV-1 or -2 RT . . . ." Office Action, p. 3.

New Claims 80-98 are definite and particularly point out that which Applicant has always considered the claimed subject matter. In particular, in the method recited in each of the claims it is explicitly indicated that the patient is an HIV-1-infected patient and that the mutation is detected in HIV-1 reverse transcriptase. As such, the above-summarized concern with respect to Claims 23-31 and 73-79 is not relevant to the definiteness of the pending claims and Applicant respectfully requests that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

II. THE REJECTIONS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 28-31 and 73 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Larder, 1992, *Antimicrob Agents Chemother*, **36**:2664-69 ("Larder"). As pointed out, above, none of Claims 28-31 and 73 are currently pending. However, for the reasons set forth below, Applicant asserts that the pending claims are not rendered obvious in view of Larder.

To reject claims in an application under 35 U.S.C. § 103, the PTO bears the initial burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); Manual of Patent Examining Procedure, Eighth Edition, August, 2001, (hereinafter "MPEP") § 2142. In the absence of establishing a proper *prima facie* case of obviousness, applicants who comply with the other statutory requirements are entitled to a patent. *In re Oetiker*, 24 USPQ2d. 1443, 1444 (Fed. Cir. 1992). In order to establish *prima facie* obviousness, the PTO must establish, *inter alia*, that the prior art, either alone or in combination, teaches or suggests each and every limitation of the rejected claims. *In re Royka* 180 USPQ 580 (C.C.P.A. 1974); *In re Wilson* 165 USPQ 494 (C.C.P.A. 1970); MPEP § 706.02(j).

New Claims 88-98 reflect that which Applicant has always considered the claimed subject matter. They clarify that the methods are directed to assessing the effectiveness of an NNRTI on an HIV-1-infected patient comprising, detecting the presence of a mutation at codon 181 of the HIV-1 reverse transcriptase, wherein the presence of such a mutation correlates with a decrease in susceptibility to delavirdine or nevirapine *and* little or no change in susceptibility to efavirenz.

Nowhere in Larder are the methods of Claims 88-98 taught, nor do any teachings of Larder suggest methods for assessing the effectiveness of an NNRTI on an HIV-1-infected patient by detecting the presence of a mutation at codon 181 of the HIV-1 reverse transcriptase, wherein the presence of such a mutation correlates with a decrease in susceptibility to either delavirdine or nevirapine *and* little or no change in susceptibility to efavirenz.

The PTO appears to base its allegations on the contention that Larder states that a mutation at codon 181 correlates with NNRTI resistance. Larder states that studies have indicated that residue 181 of HIV-1 reverse transcriptase is "critical" for the activities of diverse structures of NNRTIs (Larder, p. 2664). Applicant submits that this hypothesis, as set forth in Larder, provides what Applicant's results demonstrate is an overly simplistic approach to the relationship between a mutation at codon 181 and NNRTI resistance. The instant application shows a correlation between a mutation at codon 181 and resistance to delavirdine, to nevirapine, to delavirdine and nevirapine, but, not to efavirenz (p. 88, line 31 through p. 89, line 2, of the instant specification). Thus, as seen in the instant application as well as in Larder (page 2667, Table 5), the relationship between a mutation at codon 181 and NNRTI resistance is not as simple as the PTO or Larder's opening statements propose.

Moreover, contrary to Larder's generalization, Applicant has found that a mutation at codon 181 does not result in resistance to efavirenz. This is a surprising result and would not have been obvious to one of ordinary skill in the art, based on the teachings of Larder. This unanticipated susceptibility of residue 181 mutants to efavirenz is highly advantageous as it allows the optimization of a drug regimen of HIV-infected patients in a manner that could not have been done based on the teachings of Larder. It is noted that one of the benefits of the claimed invention is that an HIV-infected patient can continue to be treated with, or can start treatment with, efavirenz even when the HIV strain in the patient exhibits a mutation at codon 181.

Since Larder neither teaches nor suggests, for instance, a method of assessing the effectiveness of an NNRTI on an HIV-1-infected patient by detecting the presence of a mutation at codon 181 of the HIV-1 reverse transcriptase, wherein the presence of such a mutation correlates with a decrease in susceptibility to nevirapine or delavirdine and little or no change in susceptibility to efavirenz, it fails to teach or suggest each and every element of new Claims 88-98. Accordingly, Applicant submits that Larder cannot render obvious the methods of Claims 88-98.

CONCLUSION

In light of the above amendments and remarks, Applicant respectfully submits that Claims 80-98 satisfy all the criteria for patentability and are in condition for allowance. Applicant requests that the Examiner reconsider this application with a view towards allowance and solicit an early passage of Claims 80-98 to issuance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

Pursuant to 37 CFR § 1.136(a)(3), the Commissioner is hereby authorized to charge all required fees, including fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds LLP U.S. Deposit Account No. 16-1150 (order no. 011068-059-999).

Respectfully submitted,

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